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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/850,199	FILLMORE ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 03 December 2003 .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Here, claims 1-4 contain prohibited new matter. Specifically, the new phrase "non-viral" lacks any basis in the specification. A careful review by the examiner of the cited pages of the specification by the applicant failed to identify any support for this new negative limitation. The particular cited sections never use the phrase "non-viral", or specifically state that the vector is not a viral vector. As noted by MPEP 2173.05(I),

> " Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

There is no basis for the exclusionary proviso. At best, and not persuasively, Applicant's arguments would indicate that there is an absence of a positive recitation. Since no basis has been found to support the new claim limitation in the specification, the claim is rejected as incorporating new matter.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Clontech Catalog #6064-1 (pIRES-EGFP Vector Information, Copyright 1997).

Clontech Catalog #6064-1 teaches a non-viral DNA vector construct (see page 1, figure 1) comprising:

a) an internal ribosomal entry site (IRES) (see page 1, figure 1),

b) a selection marker (see page 1, figure 1,where there is an AMP selectable marker),

c) a green fluorescent protein marker (see page 1, figure 1, where EGFP is a green fluorescent protein marker).

With regard to claims 2 and 4, Clontech Catalog #6064-1 teaches "This vector can also be used to express EGFP alone or to obtain stably transfected cell lines without time consuming drug and clonal selection." Thus, Clontech Catalog #6064-1 teaches stably transfected cells with the vector of claim 1.

5. Claims 1, 2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by CLONTECHniques (April 1998).

CLONTECHniques teaches a non-viral DNA vector construct (see page 1, columns 1 and 2) comprising:

a) an internal ribosomal entry site (IRES) (see page 1, figure 2),

b) a selection marker (see page 1, figure 2,where there is an AMP selectable marker),

c) a green fluorescent protein marker (see page 1, column 2, where EGFP is a green fluorescent protein marker).

With regard to claims 2 and 4, CLONTECHniques teaches "Clontech now makes selection of stably transformed mammalian cells expressing your protein of interest more convenient with an expansion of our line of IRES Bicistronic Expression vectors (see page 1, column 3)." Thus, Clontechiques teaches stably transfected cells with the vector of claim 1.

6. Claims 1, 2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Mosser et al (Biotechniques (1997) 22(1):150-161).

Mosser teaches a non-viral DNA vector construct (see page 152, figure 1) comprising:

a) an internal ribosomal entry site (IRES) (see page 152, figure 1),

b) a selection marker (see page 152, figure 1,where there is an AMP selectable marker),

c) a green fluorescent protein marker (see page 151, figure 1, where GFP is a green fluorescent protein marker).

With regard to claims 2 and 4, Mosser teaches "In addition to the obvious utility of the dicistronic GFP plasmid for identifying clones that stably express a tTA- regulated gene product (see page 158, column 1)."

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over one of Clontech Catalog #6064-1 (pIRES-EGFP Vector Information, Copyright 1997) or CLONTECHniques or Mosser, any in view of Cheng et al (Gene Therapy (1997) 4:1013-1022).

Clontech Catalog #6064-1 teaches a non-viral DNA vector construct (see page 1, figure 1) comprising:

a) an internal ribosomal entry site (IRES) (see page 1, figure 1),

b) a selection marker (see page 1, figure 1,where there is an AMP selectable marker),

c) a green fluorescent protein marker (see page 1, figure 1, where EGFP is a green fluorescent protein marker).

With regard to claims 2 and 4, Clontech Catalog #6064-1 teaches "This vector can also be used to express EGFP alone or to obtain stably transfected cell lines without time consuming drug and clonal selection." Thus, Clontech Catalog #6064-1 teaches stably transfected cells with the vector of claim 1.

Clontechniques teaches the limitations of claims 1, 2 and 4 as discussed above.

Mosser teaches the limitations of claims 1, 2 and 4 as discussed above.

Neither Clontechniques nor the Clontech Catalog teach placement of the vector into stem cells.

Cheng teaches a DNA vector construct (see page 1014, figure 1) comprising:

a) an internal ribosomal entry site (IRES) (see page 1014, figure 1, MGIN vector with IRES element and column 2),

b) a selection marker (see page 1014, figure 1, where NEO is a selection marker in the MGIN vector),

c) a green fluorescent protein marker (see page 1014, figure 1, where EGFP is a green fluorescent protein marker).

With regard to claim 2, Cheng teaches "GFP expression in MGIN transduced TF1 cells was stable since GFP-expressing TF1 cells (which were selected either by resistance to G418 or by FACS for GFP fluorescence) continued expressing EGFP at a high level for more than 2 months in the absence of G418 selection (see page 1014, column 2)." Thus, Cheng teaches stably transfected cells with the vector of claim 1.

With regard to claim 3, Cheng teaches "We report the development of a reporter system using EGFP for the analysis of conditions leading to optimal retrovirus mediated gene transfer into human primitive hematopoietic progenitors (see page 1014, column 1)". Thus, Cheng teaches stably transfection of stem cells (see page 1015, column 2).

With regard to claim 4, Cheng teaches the reagent which is the cells as discussed in claim 2. Cheng expressly uses the reagent to study biological processes (see page 1016, column 2, subheading "Effect of GFP expression on biological properties of transduced HSPC").

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the clontech vector in the place of the Cheng vector for formation of stably transfected cells since the Clontech Catalog states "This vector can also be used to express EGFP alone or to obtain stably transfected cell lines without time consuming drug and clonal selection." Thus, an ordinary practitioner would have been motivated to use the vector of Clontech catalog in the place of the retrovirus vector where selection in a more rapid manner was performed and without a requirement for clonal selection. Further, CLONTECHniques teaches "Clontech now makes selection of stably transformed mammalian cells expressing your protein of

interest more convenient with an expansion of our line of IRES Bicistronic Expression vectors (see page 1, column 3)." So an ordinary practitioner, interested in a convenient method of expressing their protein of interest in a stable way in mammalian cells would have used the vector of CLONTECHniques. Finally, Mosser provides abundant motivation to use the dicistronic vector with the IRES-GFP element to make stable cells, including solving the "major limitation of this technology is the immense time and effort involved in the generation and screening of stable cell lines expressing a protein of interest. (see page 158, column 1)." Mosser notes that the GFP vector shown greatly simplifies the task of clone selection and eliminates the task of characterizing cell lines by standard methods (see abstract). Thus, for all of these reasons, an ordinary practitioner would have been motivated to use the IRES-GFP vectors of the prior art in any known cell line to form stable cell lines, including those of Cheng.

Double Patenting

10. Applicant's arguments, see page 6 of the response and the terminal disclaimer, filed December 3, 2003, with respect to the double patenting rejection have been fully considered and are persuasive. The rejection of claims under the double patenting rejection has been withdrawn.

Response to Arguments

11. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1634